Too much pressure in the eye is a red flag for glaucoma, a leading cause of blindness worldwide. But understanding the link between high intraocular pressure (IOP) and destruction of the optic nerve—the hallmark of glaucoma—has long bedeviled researchers who study this complex disease.

At the Jackson Laboratory in Bar Harbor, Maine, John has spent nearly two decades honing tools to illuminate glaucoma’s shad-owy corners. His lab group pioneered the development of genetic mouse models of glaucoma to study early nerve-damaging changes in the disease. And with support from a 2008 Hughes Collaborative Innovation Award, they are creating the ultra-miniature device to continuously mon-titor IOP inside a mouse eye.

His team recently revealed the role of inflammation and the immune system in causing damage to the optic nerve. In response to early tissue stresses, a class of immune cells known as monocytes seep into the optic nerve at the earliest stage of the disease, before any damage can be detected. The discovery supports a growing belief that neuroinflammation—an inflammatory response to stress or injury in neural tissues—is a primary cause of glaucoma, John says.

Another key finding, described April 2, 2012, in the Journal of Clinical Investigation, offers clues to a potential treatment for glaucoma. A single, targeted x-ray treatment to the eye of a glaucoma-prone mouse provided long-term protection against the disease in that eye.

The idea to test radiation arose from an earlier study that used whole-body radiation when replacing the bone marrow in glaucoma-prone mice. Normally, about 80 percent of these mice develop glaucoma. But in John’s study, 96 percent of the irradiated mice had no evidence of it. “The magnitude of the effect was so large, it was almost unbelievable, so we did the experiment three more times to make sure it was correct,” John says.

The radiation, they found, changes the expression of genes in the endothelium, the thin layer of cells lining blood vessels. The endothelium controls monocyte movement into the optic nerve, so blocking that route may be one explanation for the protection, though other, as-yet-unidentified factors may be involved as well. Radiation per se might not prove a practical treatment, John says, but the finding may aid in creating other neuroprotective therapies.

A Wireless Sensor

Importantly, the radiation treatment does not alter IOP. Clarifying the role of this key risk factor remains a challenge. As John explains, current methods for measuring eye pressure are inadequate; they cannot provide around-the-clock data, and pressure can vary considerably during a day. A snapshot measurement taken just once a day, for example, is not enough to accurately relate pressure effects to neural damage. Additionally, repeatedly disturbing a mouse to measure pressure may alter the disease process. That’s where the tiny IOP sensor may help.

Purdue University engineers Pedro P. Irazoqui and William J. Chappell created the device, which incorporates a silicon chip, a pressure sensor, and an antenna.

“I challenged Pedro and Bill, and they came up with some remarkable innovations
to allow miniaturization of the devices,” John says. For example, the engineers developed special glue embedded with gold-coated nickel beads that conduct electricity, but only in the desired direction. The glue binds the components together. No need for wires.

The silicon chip processes data from the sensor, and both are powered by radiofrequency waves sent via an external transmitter to the antenna. The device then automatically sends the information to a receiver outside the cage. The team is close to having a fully functional prototype, John says. Once that happens, they hope to move the hand-built device to a commercial developer to produce it for research laboratories worldwide.

By providing more detailed information on how IOP changes over time, the device will enable researchers to relate those changes to optic nerve damage, John says. “That, in turn, will allow us to identify new mouse models for glaucoma far more easily and accurately, which will have a revolutionary effect on our ability to understand the genetics and molecular mechanism of glaucoma.”

John also envisions the monitor helping develop treatments. “For example, a sensor could measure pressure and then wirelessly send that data to a miniature pump, which would then deliver a drug as needed, based on biofeedback. These are the types of things we’re thinking about and hope to test in the future.”

— JULE CORLISS